mycosis fungoides. The significance of the different clinical patterns is not clear at present, but it seems likely that "lymphomatoid papulosis" is not a single disease entity. The application of recently developed immunological methods may help to better define the nature of these perplexing eruptions and their relationship to lymphoid neoplasia.

At present there is no specific therapy for these eruptions and it is clear that these patients should be kept under periodic observation.

DAVID G. DENEAU, MD

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Inflammatory Lesions of Acne Vulgaris: Current Concepts

PATHOGENIC MICROORGANISMS are not commonly present in the inflammatory lesions of acne, and the microorganisms that are present do not invade and multiply in the tissues. Thus, these inflammatory lesions do not involve an infection in the usual sense.

Minor inflammatory lesions are small, very superficial, immediately perifollicular and intrafollicular, short-lived and usually heal without scarring. Such lesions may be benefited by topical therapy. They appear to be the consequence of polymorphonuclear leukocyte aggregation in response to chemotactic factors in the follicle.

Major inflammatory lesions begin deeper (in the dermis), forming nodules of varying size and severity, often persisting for a long time. The crucial event responsible is disruption of the follicle wall with escape of follicle contents into the dermis. The contents include disintegrated epithelial and sebaceous cells, sebum in varying stages of chemical change, microflora including anaerobic *Propionibacterium acnes,* aerobic *Staphylococcus epidermidis,* yeasts, metabolites of these organisms (lipase, proteases and others), free fatty acids, squalene, keratin and hair fragments. Many of these are antigenic and when combined with lipids with adjuvant properties, have the potential for induction of immune reactions. Others can cause primary irritation and foreign body reactions. Thus, the follicle contents include a variety of possible pathogenic agents.

Histologically, the major lesions present elements of mixed granuloma, and infiltrates of polymorphonuclear leukocytes, histiocytes, macrophages and lymphocytes. Fibroblasts and newly formed capillaries are commonly observed. Vasculitis is not present. Hemorrhage and necrosis with ulceration may occur and scarring can be severe.

To prevent the occurrence of major lesions it is necessary to block those mechanisms which disrupt the follicle wall. A frequent finding in early lesions is the invasion of the follicle wall by polymorphonuclear leukocytes with abscess formation. Release of lytic and toxic agents, which may damage the wall, would be a likely consequence. The concept that obstruction of the follicle ostium with subsequent build up of sebum, formation of a comedo, and pressure rupture of the follicle is untenable because it has been shown that disruption occurs in follicles in which obstruction and gross comedones are not present.

In view of the nature of the lesions and the absence of active infection, it is not unexpected that antibacterial agents exert no major beneficial effect on existing inflammatory lesions, and there are no controlled data to show that they do. To the extent that they are effective, it is by decreasing the occurrence of new lesions. Presumably, the mechanism is by reduction of the bacterial population of susceptible follicles.

Existing inflammatory lesions do respond to nonspecific antiinflammatory agents, particularly corticosteroids, either by local or systemic routes of administration. When severe lesions in great numbers are present, systemic therapy is required. In certain cases, for reasons unknown, intensely inflammatory lesions supervene in what had been mild and not otherwise unusual acne vulgaris. The lesions are characterized by pain, hemorrhage, sterile suppuration, gelatinous granulation tissue, liquifying necrosis, ulceration and severe scarring. In some instances the onset has been preceded by viral infections, measles and infectious mononucleosis, or periods of extreme emotional stress. In many cases, no trigger factors are recognized. The nature and pathogenesis of the lesions have not been clarified.

This subject was comprehensively reviewed by Goldschmidt and co-workers in a report in 1977. Systemic corticosteroid therapy was necessary for control. Most cases reverted to their previous state

of relatively mild inflammatory acne after corticoid therapy, suggesting the possibility of altered reactivity.

JUD R. SCHOLTZ, MD

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Update on the Use of Retinoids

THE TERM RETINOID refers to vitamin A in all its naturally occurring forms, as well as to the various synthetic analogues that have been developed. Various retinoids, particularly transretinoic acid, vitamin A alcohol (retinol) and certain retinol esters, have been used by dermatologists for many years in the treatment of several cutaneous disorders, especially those characterized by abnormal keratinization. However, the clinical usefulness of these older derivatives has been limited by their side effects. Common side effects resulting from therapeutically useful dosages of transretinoic acid include headache, anorexia, flushing, fatigue and dryness of the lips and skin. Less common side effects include nausea, polydipsia, dizziness, petechiae, loss of hair, increased perspiration, dryness of nasal mucosa, dandruff, psychological disturbances, facial edema and changes in pruritus. In addition, chronic vitamin A excess has been noted to cause joint and bone pain, prominence and irritation of the eyes, hepatomegaly, splenomegaly, urinary frequency and urgency, and increased intracranial pressure with concurrent neurological signs (more common in children and adolescents). In contrast to the poor therapeutic index of the older retinoids, some of the newer derivatives, especially 13-cis-retinoic acid and an aromatic retinoic acid derivative RO 10-9359, appear to be more effective with less toxicity.

Complete to nearly complete clearing (greater than 90 percent) in patients with lamellar ichthyosis, pityriasis rubra pilaris and keratosis follicularis has been reported in recent trials with the use of these new retinoids. However, data concerning relapse after discontinuing therapy, as well as ideal initial dosage and dosages for maintenance therapy, have not yet been determined.

Several investigators have also reported the clinical usefulness of RO 10-9359 in the treatment of psoriasis. In many trials, about 50 percent of the patients treated have had good to complete clearing. It is noteworthy that most patients chosen for these trials have severe chronic psoriasis and are often recalcitrant to conventional therapy. This new aromatic retinoid also appears to be effective in erythrodermic and pustular psoriasis. It has been shown to be an effective oral adjuvant in psoriasis therapy, increasing the clinical efficacy of more conventional treatment regimens such as topical anthralin, ultraviolet B (UVB) radiation, and psoralen combined with ultraviolet A (UVA) radiation.

The derivative 13-cis-retinoic acid has been used effectively in the treatment of cystic and conglobate acne. Peck and co-workers reported complete clearing in 13 of 14 patients with resistant cystic and conglobate acne who used 13-cis-retinoic acid. It is significant that prolonged remissions were observed in all the patients treated, lasting as long as 20 months after discontinuation of therapy.

Finally, preliminary investigations indicate that the new retinoids may be effective in the treatment of basal cell carcinomas. Peck and co-workers treated 11 patients with multiple basal cell carcinomas induced by sunlight, irradiation, arsenic or the basal cell nevus syndrome. Orally given 13-cis-retinoic acid was used and of the 248 tumors treated, 39 (16 percent) underwent complete clinical regression. Biopsy specimens were obtained after treatment for 35 of the 39 tumors; 21 of them showed complete histological clearance. Of the remaining tumors, 162 (65 percent) decreased in size and 47 (19 percent) were unchanged after treatment.

With regard to toxicity, it appears that the adverse effects observed with these two new retinoids are usually mild and rarely, if ever, severe enough to discontinue therapy. The most common side effects noted have been limited primarily to the skin and mucous membranes, which can result in various minor disturbances such as cheilitis, facial dermatitis, xerosis, dry nasal mucosa, minor nosebleeds, conjunctivitis, increased skin fragility, inflamed urethral meatus, paronychia, hair thinning, dry hair and a palmo-plantar desquamation. Other less common side effects include changes in appetite, increased thirst, headache and arthralgias without evidence of arthritis. Temporary slight elevations of the serum transaminases have also been observed in patients receiving the new retinoids. According to Peck and co-workers, this occurs in 10 percent to 15 percent of patients, but the importance of these changes is unclear because